

Claims

1. A pharmaceutical composition for altering cellular responses to TGF β s and/or BMPs; the composition comprising a molecule which prevents, inhibits or reduces the association of a Smad protein with a UCH, or a nucleic acid construct directing the expression of such a molecule, in admixture with a physiologically acceptable carrier, excipient or diluent.
2. A composition according to claim 1, wherein the composition prevents, inhibits or reduces the association of a Smad3 protein with a UCH.
3. A composition according to claim 1 or 2, wherein the composition prevents, inhibits or reduces the association of a Smad protein with UCH37.
4. A composition according to any one of the preceding claims, wherein the composition comprises, as an active agent, a molecule which comprises a structural analogue of the UCH-binding site of a Smad protein.
5. A composition according to any one of claims 1-3, wherein the composition comprises, as an active agent, a molecule which comprises a structural analogue of the Smad-binding site on a UCH protein.
6. A composition according to any one of claims 1-4, wherein the active agent comprises a peptide of at least 8 amino acid residues which exhibits at least 60% identity, preferably at least 70%, more preferably at least 80%, and most preferably at least 90% identity, with a contiguous portion of a Smad polypeptide; or a nucleic acid construct directing the expression of such a peptide.
7. A composition according to claim 6, wherein the peptide comprises at least 10 residues.

8. A composition according to claim 6, wherein the peptide comprises at least 12 amino acid residues.
9. A composition according to claim 6, wherein the peptide comprises at least 15 amino acid residues.
10. A composition according to any one of claims 6-9, wherein the peptide comprises fewer than 80 amino acid residues.
11. A composition according to claim 10, wherein the peptide comprises fewer than 60 amino acid residues.
12. A composition according to claim 10, wherein the peptide comprises fewer than 40 amino acid residues.
13. A composition according to any one of claims 6-12, wherein the peptide exhibits at least 60% sequence identity with a contiguous portion of Smad3.
14. A composition according to any one of claims 6-13, wherein the peptide exhibits at least 60% identity with a contiguous portion of Smad3 present within amino acid residues 114-240 thereof.
15. Use of a substance which prevents, inhibits or reduces the association of a Smad protein with a UCH, in the preparation of a medicament to cellular responses to TGF β s and/or BMPs.
16. Use of a substance, in accordance with claim 15, in the preparation of a medicament in accordance with any one of claims 1-14.

17. A method of altering cellular responses to TGF β s and/or BMPs, the method comprising the step of introducing into a cell a molecule which prevents, inhibits or reduces the association of a Smad protein with a UCH.
18. A method according to claim 17, which comprises the step of administering a composition in accordance with any one of claims 1-14.
19. A method of screening a test substance for the ability to prevent, inhibit or reduce the association of a Smad protein with a UCH, the method comprising the step of contacting the test substance with a Smad protein and/or a UCH and determining, qualitatively or quantitatively, the amount of association of the Smad protein with the UCH when these are contacted.
20. A method according to claim 19, wherein at least one of the test substance, Smad protein and UCH is labelled with a readily detectable label.